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| 09/725,010 | 11/29/2000 | Paula Sundstrom | 23878.0005 | 8550 |

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| EXAMINER |
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ZARA, JANE J

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| ART UNIT | PAPER NUMBER |
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1635

DATE MAILED: 07/02/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.
09/725,010

Applicant(s)
Sundstrom

Examiner
Jane Zara

Art Unit
1635



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Jul 25, 2002
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-43 is/are pending in the application.
- 4a) Of the above, claim(s) 8-10, 12-18, 22-26, and 33-43 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7, 11, 19-21, and 27-32 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 11/29/06 is/are a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 2,3
- 4) ☒ Interview Summary (PTO-413) Paper No(s). 10
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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DETAILED ACTION

This Office action is in response to the communication filed July 25, 2003.

Claims 1-43 are pending in the instant application.

Election/Restriction

The non-responsive notice mailed January 13, 2002, Paper No. 9, has been vacated and an examination on the merits of elected Group III and SEQ ID NO: 1 are set forth below.

Claims 8-10, 12-18, 22-26, and 33-43 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 5.

Applicant's election with traverse of Group III, in Paper No.5 is acknowledged. The traversal is on the ground(s) that the inventions of the different groups are not patentably distinguishable inventions and furthermore do not pose a serious burden to examine all of the groups claimed. This is not found persuasive because the groups I, II, IV-XI comprise various patentably distinct methods utilizing different and distinct steps not utilized in the method of elected group III. The methods of the non-elected groups include manipulating environmental factors, manipulating signal transduction pathways, manipulating expression of DNA binding proteins, manipulating DNA binding protein binding activities, interfering with the expression of regulatory proteins of DNA binding proteins, inhibiting cell growth of a fungus in a patient, inhibiting genes essential for fungus adhesion and characterizing genes under control of DNA

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binding proteins. Proper examination of each of these different and distinct methods, as well as examination of the composition claim of group X, drawn to nucleic acid compositions, would require searches of prior art that are neither coextensive nor overlapping and would therefore require a serious burden to the examiner and the searching facilities of the PTO.

Applicants argue that a *prima facie* instance of serious burden only exists when separate classifications are shown. This is not found persuasive because the broad classifications encompassed within the various classes and/or subclasses (e.g. class 435, subclass 6, encompassing measuring or testing processes involving nucleic acids) cover extensive subject matter and do not necessarily reflect appropriate, accompanying search burdens.

Applicants' election with traverse in Paper No. 5 of HWP1, NIT2 binding site and DNA binding protein GAT99 is also acknowledged. Elected Group III and elected species HWP1, NIT2 binding site, and DNA binding protein GAT99, of claims 1-7, 11, 19-21 and 27-32 have been examined on the merits as indicated below.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 1-7, 11, 19-21, 27-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method for interfering with expression of any hyphal-specific gene in a fungus resulting in inhibition of cell growth of the fungus, comprising interfering with transcription of hyphal specific genes mediated by any cis acting sequence or sequences, and which cis acting sequences comprise cis regulatory elements including upstream activating sequences (UAR) or upstream repressing sequences (URS), and which interfering steps comprise interfering with any DNA BP binding to any cis regulatory elements. The specification and claims do not describe the elements that are essential to the broad genus comprising hyphal specific genes, nor of cis acting sequences comprising cis regulatory elements, including UAS and UAR elements, nor of DNA binding proteins that bind to the claimed cis regulatory elements. In addition, the specification and claims do not describe the broad genus comprising any insertions, deletions, mutations or modifications of the hyphal specific sequence of SEQ ID NO: 1. The specification and claims do not indicate what distinguishing attributes are concisely shared by members of the broad genera comprising cis acting sequence comprising cis regulatory elements of any and/or all hyphal specific genes in a fungus, nor of the mutations, deletions, insertions or modifications to SEQ ID NO: 1. Nor has adequate description of hyphal specific genes comprising genes responsible for controlling dimorphism been provided in the instant disclosure.

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The specification does not place any limit on the number of nucleic acid or amino acid substitutions, deletions, insertions and or modifications to SEQ ID NO: 1. No common structural attributes identify the members of the broad genera claimed. The scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number structural differences between genus members is permitted. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics concisely identifying members of the proposed genus, and because the genus is highly variant, the description provided for defining genus members is insufficient. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the broad genera claimed. Thus, applicant was not in possession of the claimed genus.

Claims 1-7, 11, 19-21, 27-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for measuring expression patterns of HWP1 mRNA and HWP1 protein in fungus compared to the expression of housekeeping genes such as enolase, does not reasonably provide enablement for the ability to interfere with the expression of any and/or all hyphal specific genes in a fungus by interfering with transcription of hyphal specific genes mediated by any and/or all cis acting sequences. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

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The claims are drawn to methods for interfering with expression of any and/or all hyphal-specific genes in any fungus resulting in inhibition of cell growth of the fungus, comprising interfering with transcription of any and/or all hyphal specific genes mediated by any and/or all cis acting sequences, and which cis acting sequences comprise cis regulatory elements including upstream activating sequences (UAR) or upstream repressing sequences (URS), and which interfering steps comprises interfering with any DNA binding protein (DNA BP) that binds to the cis regulatory elements.

The state of the prior art and the predictability or unpredictability of the art. The participation of hyphal specific genes in fungal infections is under investigation in many laboratories and has been found to involve multiple cascades and regulatory mechanisms. Csank et al ("BO" submitted in IDS, Paper No. 3, March 29, 2001) teach the involvement of regulatory kinase cascades in fungi which regulate transcription factors controlling developmental processes (e.g. see text on page 2713; text and figure on page 2719). Csank et al also report the retention of normal hyphal development of null mutants of MAPK cascade regulated transcription factor, Cph1p, illustrating the complexity and unpredictability of the involvement and roles various cascades and molecular components in hyphal development (see page 2720). Braun et al ("BE" submitted in IDS, Paper No. 3, March 29, 2001) also teach of the complexity of hyphal development and the inability to predict the role of various molecular players when deletion of the TUP1 gene, a general transcriptional repressor, led to the surprising lack of response to known growth inducers (see page 107, first full paragraph in right column). In addition, Bernardis et al

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("BS" submitted in IDS, Paper No. 3, March 29, 2001) teach the versatility of *C. albicans* in its ability to cause both systemic and mucosal infections as a symbol of the fungus' ability to express quite different survival factors for specific adaptation requirements (see generally the text on pages 201 and 205). These studies collectively suggest that the field of transcriptional regulation of hyphal specific genes is still in its infancy and hence highly unpredictable at the current time.

The amount of direction or guidance presented in the specification AND the presence or absence of working examples. Applicants have not provided guidance in the specification toward a method of interfering with the expression of any and/or all hyphal specific genes in any fungus resulting in the inhibition of cell growth of said fungus by interfering with transcription of any and/or all hyphal specific genes mediated by cis acting sequences.

The specification teaches a difference in the expression of HWP1 in *C. Albicans* compared to the housekeeping gene *enol*. The specification also teaches the presence of purported cis regulatory sequences in the promoter region of HWP1 of SEQ ID NO: 1 by alignment of SEQ ID NO: 1 with fungal matrices using MatInspector v2.2. The specification, however, fails to teach a method of interfering with expression of any and/or all hyphal specific genes in any fungus resulting in inhibition of cell growth of the fungus comprising interfering with the transcription of any and/or all genes mediated by any and/or all cis acting sequences. One skilled in the art would not accept on its face the examples given in the specification of purported cis acting sequences

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identified by sequence alignment as being correlative or representative of the ability to interfere with any and/or all hyphal specific genes in any fungus, whereby fungus growth is inhibited in view of the lack of guidance in the specification and known unpredictability associated with the transcriptional regulation of hyphal specific genes in fungus. The specification as filed fails to provide any particular guidance which resolves the known unpredictability in the art associated with the transcriptional regulation of any and/or cis acting sequences in any and/or all hyphal specific genes in any fungus.

The breadth of the claims and the quantity of experimentation required. The breadth of the claims is very broad. The claims are drawn to methods for interfering with expression of any and/or all hyphal-specific genes in any fungus resulting in inhibition of cell growth of the fungus, comprising interfering with transcription of any and/or all hyphal specific genes mediated by any and/or all cis acting sequences, and which cis acting sequences comprise cis regulatory elements including upstream activating sequences (UAR) or upstream repressing sequences (URS), and which interfering steps comprises interfering with any DNA binding protein (DNA BP) that binds to the cis regulatory elements. In order to practice the invention over the scope claimed, it would require undue trial and error and undue experimentation beyond which is taught in the specification to practice the invention drawn to the inhibition of cell growth in any fungus comprising the interference of transcription of hyphal specific genes mediated by cis acting sequences. The quantity of experimentation required to practice the invention as claimed would require the *de novo* determination of the cis acting sequences mediating any and/or all hyphal

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specific genes in any fungus, whereby interference with their expression results in the inhibition of cell growth of the fungus. Since the specification fails to provide any particular guidance for the inhibition of cell growth of any and/or all fungus by interfering with the expression of any and/or all hyphal specific genes mediated by cis acting sequences, and since determination of the factors required for interfering with any and/or all hyphal specific genes whereby fungus cell growth is inhibited is highly unpredictable, it would require undue experimentation to practice the invention over the scope claimed.

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Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is (703) 306-5820. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (703) 308-0447. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (703) 305-3413. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JZ

June 16, 2003


KAREN LACOURCIERE
PATENT EXAMINER